

**METHOD FOR THE ANODIC ALKOXYLATION
OF ORGANIC COMPOUNDS**

[0001] The invention is aimed at a method for anodic alkoxylation of organic
5 compounds, particularly cyclic ethers, N-substituted amides, carbonyl compounds,
alkylaromatic and alkylheteroaromatic compounds. The anodic alkoxylation, particularly if it
is a methoxylation, is carried out in an electrolysis cell divided by a membrane electrode
assembly (MEA) in the absence of a mediator.

[0002] Alkoxylation reactions of saturated and unsaturated cyclic ethers and of
10 N-alkylamides and alkylaromatic and alkylheteroaromatic compounds are industrially
important since the resulting products or their hydrolysis products are valuable raw materials
for pharmaceuticals and pesticides. Various methods are known for anodic alkoxylation of
organic compounds.

[0003] US Patent 2,714,576 teaches the electrolytic production of
15 2,5-dialkoxy-2,5-dihydrofurans, where furan or a substituted furan is electrolyzed in an
aliphatic alcohol with 1-5 carbons in the presence of a soluble electrolyte. The electrolyte that
is used is ammonium bromide, the effect of which is that it acts as a mediator. The substrate
to be alkoxyated is thus not directly alkoxyated, but rather indirectly alkoxyated, namely
via the intermediate step of bromination. An important disadvantage of anodic alkoxylation
20 in the presence of a mediator, in particular a halogen compound, is that the mediator itself can
lead to increased formation of byproducts and accordingly makes the processing and
purification of the alkoxyated substrate more difficult.

[0004] Anodic alkoxylation of furan derivatives in the presence of conductive salts
that do not act as mediators, for example alcoholates, is known, but with such methods the
25 efficiencies [current yields] and product yields are, for the most part, very low.

[0005] In the desire to make further improvements in the alkoxylation of organic
substrates like furans and N-alkylamides, methods were developed that do without
conductivity-increasing additives, but in which a solid electrolyte (solid polymer electrolyte =
SPE) is used instead. The solid electrolyte in this case is expediently in the form of a
30 membrane, where the two sides of the membrane are in close contact with the electrodes. The
membrane, anode and cathode thus form a so-called membrane electrode assembly (MEA).

[0006] In Dechema Monographie, Volume 112, 299-315 (1988), Fabienke et al. described organic chemical syntheses, including the methoxylation of furan, in flow-through cells with a membrane electrode assembly of an ion exchanger membrane with porous catalytic electrodes on both sides of the membrane. The electrode reaction here takes place at catalyst layers on the membrane surface. The current is supplied through suitable current collectors; the swollen ion exchanger membrane acts as an ion conductor. According to the teaching of this document, the electrocatalytic layers can be applied directly to the membrane (attached porous electrode layer), or porous, possibly coated electrodes can be pressed against the membrane without a spacing (zero gap). The electrode layers for alkoxylation in this document were porous platinum layers electrochemically applied to a polyfluorinated cation exchanger membrane.

[0007] While the efficiencies and the stability of the porous platinum layers were characterized as good in the document just mentioned, Ogumi et al., Nippon Kagaku Kaishi 11, (1984) 1788-1793, came to a different result in the alkoxylation of furan using a similar membrane electrode assembly, since only low efficiencies were obtained. The efficiency can be increased and the voltage clearly reduced by adding a small amount of bromine. Since bromine is a difficult mediator, the known disadvantages cannot be overcome with this method. Since Fabienke et al. on the one hand and Ogumi et al. on the other came to completely different results, it must be presumed that the structure of the membrane electrode assembly and/or the manner of applying the electrode layers have a considerable effect on the alkoxylation of furan.

[0008] Jörissen et al. reported in Dechema Monographie Volume 125 (1992), 993-706, on the use of fuel cells with a membrane electrode assembly for conducting organic reactions, including the methoxylation of furan. The membrane electrode assembly is a Nafion® membrane (sulfonated polyfluorinated polymer or copolymer from E. I. DuPont company) chemically or electrochemically deposited on the surface. Platinum/iridium gauzes or graphite felt are used as collectors. High efficiencies can be obtained in the alkoxylation of furan only if very high cell voltages are applied, which is, however, very disadvantageous with regard to a larger plant.

[0009] In his dissertation (Dortmund University, October 14, 1999) D. Klein carried out research on the use of conducting electrolyte-free SPE electrosyntheses in non-aqueous

systems and used the SPE fuel cell technology here for methoxylation of carboxylic acid amides and furan. The electrocatalyst layer of the membrane electrode assembly was situated on or within the surface of the Nafion® membrane. The electrocatalyst layer in this case was either deposited as a porous layer on the Nafion® membrane by a chemical/electrochemical process or prepared by an indirect printing process and pressed onto the membrane. In the indirect process the electrocatalyst was dispersed in a Nafion® solution and this mixture was applied to a Teflon film; after evaporation of the solvent mixture at elevated temperature, the catalyst layer including the carrier film was pressed onto the membrane by means of a hot press; then the carrier film was peeled off. In the methoxylation of furan without additives the cell voltage rose to impossibly high values within a very short time. This electrosynthesis could be improved through the addition of various cosolvents, but this makes the processing of the reaction mixture more difficult. The statements in this document allow the suggestion that the type of electrocatalyst layer is a source of the unsatisfactory behavior of the electrosynthesis in the absence of cosolvents.

[0010] In the methods in accordance with DE 195 33 773 A1 and EP 0 965 658 A1, EP 0 965 659 and EP 0 965 660 a stacked plate cell with series-connected stacked electrodes is used for electrolytic oxidation, including anodic alkoxylation of alkylaromatic compounds, ethers and carboxylic acid amides, where at least one stacked electrode consists of a graphite felt plate, a carbon felt plate or a fabric of a carbon coated educt contact surface. Expediently, the electrolyte phase in contact with the carbon-containing stacked electrodes is a solid electrolyte. The technical cost of the stacked plate cell is considerable, since the cell demands specific construction and suitable periphery. Although high selectivities can be achieved in some cases, the efficiencies leave something to be desired. There is thus a potential for further improvement.

[0011] In the GDCH Monographie, Volume 23 (2001), 241-249, Reufer et al. reported on the methoxylation of furan in a fuel cell as synthesis reactor. A membrane electrode assembly based on a Nafion® membrane that was coated on both sides with carbon black was used. A membrane that was coated with platinum-modified carbon black was also used in some cases. Commercial graphite paper was used as current collector. A rapid rise of voltage was observed in the methoxylation of furan using a membrane coated on both sides with carbon black. A better course of the voltage over the electrolysis time could be achieved

by applying platinum to the carbon black-coated membrane, but the furan conversion and product formation were adversely affected by the platinum. Although it was stated in this document that the internal structure of the electrolysis appears to have an effect on the efficiency of the electrolysis, neither data on the composition of the carbon black coating nor data on the method by which the coating was applied to the membrane were given. Thus, there is an additional high interest in making further improvement to the alkoxylation of substrate that is known from a number of documents.

[0012] WO 97/13006 teaches a membrane electrode assembly that has an oxidizing catalyst on one side of a polymer perfluorosulfonic acid membrane and a reducing catalyst on the other side, which contains at least one of the following elements in elemental form or in the form of compounds, specifically Zn, La, Ce, Pr, Nd, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lo, Bi and In. The oxidizing catalyst expediently contains an element from among palladium, platinum and iridium. The membrane electrode assembly is prepared by direct coating with a suspension that contains a catalyst-containing carbon black and an ionomer binder in a liquid medium like propylene carbonate. Besides the said membrane electrode assembly and a reactor containing it, the said document is aimed at a method for producing hydrogen peroxide from hydrogen and oxygen. Moreover, alkenes can be epoxidized and sulfur dioxide can be oxidized to sulfuric acid using a membrane electrode assembly with the said reducing catalyst. The conversion of organic nitro compounds to amine dyes and the recovery of phenol from benzene are mentioned as other possible areas of use. There are no indications of conducting other reactions than those mentioned and/or using a membrane electrode assembly that has a reducing catalyst different from the said catalyst in this document.

[0013] Accordingly, the object of this invention is an improved method for alkoxylation of organic compounds, particularly those from among the cyclic ethers, N-substituted amides, carbonyl compounds, especially ketones, alkylaromatic compounds and alkylheteroaromatic compounds, where the anodic alkoxylation can be carried out with high efficiency in an electrolysis cell containing a membrane electrode assembly in the absence of a mediator. According to the preferred embodiment the anodic alkoxylation should be carried out under practical operating conditions at a cell voltage under 25 volts.

[0014] It was surprising to find that the said task and additional tasks, as follow from the description given below, can be solved by the fact that a membrane electrode assembly that has a coating containing carbon black and/or graphite on both sides of a fluorinated cation exchanger membrane or a nonionomeric microporous polypropylene membrane, which
5 coating additionally contains an ionomer in addition to the carbon black or graphite and optionally a heavy metal catalyst, is used as membrane electrode assembly.

[0015] Accordingly, a method was found for anodic alkoxylation of an organic compound, in which a mixture containing the organic compound and an alcohol with 1 to 4 C atoms, especially methanol or ethanol, is passed through the anode space of a reactor divided
10 into an anode space and a cathode space by means of a membrane electrode assembly (MEA) and where the MEA consists of a membrane that is provided on both sides with an electrode layer, which is characterized by the fact that a reactor having an MEA with a cation exchange membrane or a microporous polypropylene membrane, one or both electrode layers of which were produced using a carbon black and/or graphite, which may be doped with a heavy
15 metal, and a sulfonated polyfluorinated polymer or copolymer in a suspension containing a liquid suspension medium, is used.

[0016] The dependent claims are aimed at preferred embodiments of the method in accordance with the invention, particularly embodiments of the coating and of the organic substrates that are preferably to be alkoxylation. In the case of alkoxylation with isopropanol,
20 one must take into account that the stability of a Nafion® membrane is limited in this medium.

[0017] The construction of a reactor with a membrane electrode assembly (MEA) is well known to the specialist: the reactor consists of a vessel that is divided into a cathode space and an anode space by an MEA arranged in it. On each side of the MEA there are
25 microporous current collectors, which, like the actual electrode layers, are permeable to matter. The current collectors consist of an electrically conductive porous material, for example a graphite paper, graphite felt or a gauze of a noble metal or metal alloy. The current collector layer lying opposite the electrode layer is adjacent to the cathode space or the anode space. Expediently, these spaces are designed in the form of a structured flow field, which
30 can be parallel channels, meandering channels or a checkerboard structure that enables

crossmixing. The reactor also includes an inlet and outlet into/out of the cathode space and into/out of the anode space.

[0018] In the alkoxylation of an organic compound the compound to be alkoxyated is passed through the anode space in a solution of the alcohol that is used for alkoxylation. If
5 necessary, known auxiliary agents can be added to the solution to stabilize the course of the voltage in amounts that are effective but that do not significantly lower the selectivity.

Examples are water and H_2SO_4 . Solutions with a cosolvent like sulfolane or alkylamides can also be used. The reaction mixture that is being alkoxyated or an already alkoxyated reaction mixture can be used to transport the hydrogen that forms at the cathode away.

10 Alternatively, especially in continuous processes, it is also possible to use other liquid media or a gaseous medium that contains components through which the efficiency of the membrane is not adversely affected as cathode space medium. According to an especially preferred embodiment the mixture to be alkoxyated is first sent through the anode space and then also sent through the cathode space. After the separation of the hydrogen from the at
15 least partially alkoxyated reaction mixture the latter can be again sent through the anode space. This circulation process is repeated until the desired conversion of the compound being alkoxyated, or the desired charge conversion is achieved. The processing of the alkoxyated reaction mixture is governed by the material data of the reaction components contained in it. Usually the processing consists of steps that include distillation and
20 extraction.

[0019] Surprisingly, the alkoxyated end products proved to be suitable solvents for increasing the selectivity. Accordingly, it can be advantageous to add up to 35 mol% of the alkoxyated product to the feed mixture at the beginning of the electrode synthesis.

[0020] The anodic alkoxylation, particularly if it is a methoxylation or ethoxylation,
25 is expediently carried out at a current density in the range of 1-500 mA/cm^2 , preferably 10-50 mA/cm^2 . The reactor is operated at a voltage in the range of 1-50 volts, preferably 5-25 volts. The input concentration of the compound being alkoxyated in the alcohol that is used for alkoxylation is not very critical; preferably at an input concentration in the range of 0.1-5 mol/L, especially 0.5-3 mol/L is preferred.

30 [0021] The membrane (MEA) is preferably an ionomer membrane with cation exchanger properties. In view of the necessary chemical stability of the membrane,

fluorinated membranes that contain sulfonic acid groups as cation exchange groups have proven to be suitable. Preferred polymers and copolymers can contain, besides a carbon chain that forms a polymer chain, chain elements or branchings that contain ether bridges.

Polymers and copolymers of this kind are commercially available in the form of films, for example under the name Nafion® (E. I. DuPont) and Gore Asselext® (W. L. Gore and Associates). The solid electrolyte formed as membrane of the MEA can consist of one or more layers and preferably has a thickness in the range of 25-300 µm.

[0022] Surprisingly, microporous nonionic membranes, especially microporous polyolefin membranes such as, preferably, a polypropylene membrane, are also suitable. The selectivity of the alkoxylation using the microporous polypropylene membrane that was used by the inventors is somewhat lower than is the case when using an ionomer membrane, but the chemical stability of the membrane is considerably higher than that of the Nafion® membranes.

[0023] Any sufficiently conductive carbon black or graphite that is known for such purposes or any mixture of carbon black and graphite can be used to make the electrode layers. The carbon black or graphite that is used can be doped with an effective amount of a catalytically active heavy metal, especially a metal from among gold, platinum, palladium and iridium. The suspension used to produce the electrode layers contains, besides the carbon black or the doped carbon black and ionomeric, especially a polyfluorinated sulfonated polymer or copolymer in dissolved form or in the form of swollen, very small particles. Solvents or swelling agents can be used in pure form or in the form of mixtures. Suitable agents are, for example, alcohols like isopropanol, isobutanol and tert-butanol, and esters, especially cyclic esters like propylene carbonate. Dissolved binders based on perfluorinated sulfonated polymers and copolymers that can also be further diluted with the said solvents are commercially available. Ionomers in Na⁺ form are available in aqueous solvent systems. The polymer or copolymer in dissolved form is mostly not in the form of the free sulfonic acid, but rather in the form of salt, for example a sodium salt or preferably a tetrabutylammonium salt. The solution of the polymer or copolymer can additionally contain water.

[0024] The suspension is used in a substantially known way utilizing conventional coating techniques like spreading, printing, immersion and spraying to generate the porous

electrode layers. As an alternative to these techniques the indirect printing process is also a possibility, where first an inert carrier is coated and then the layer is transferred to the ionomer carrier. Coating by screen printing is especially expedient. After coating the membrane with the suspension the solvent containing the suspension is evaporated at
5 elevated temperature and then the membrane together with the electrode layer or with the two electrode layers is subjected to heat treatment at a temperature in the range of 75°C to about 85°C. After the temperature treatment the electrode layer, if it was in salt form, is converted to the protonated form in a substantially known way. The method for producing the membrane electrode assembly with the generic electrode layers is disclosed in US patent
10 5,211,984, which is hereby incorporated into the description.

[0025] In particular organic compounds from among the cyclic ethers, N-substituted amides, carbonyl compounds such as especially ketones, alkylaromatic compounds and alkylheteroaromatic compounds, can be subjected to the anodic alkylation in accordance with the invention.

15 [0026] A first class of readily alkoxyated substrates consists of cyclic ethers, which can be saturated, unsaturated or heteroaromatic. The oxygen-containing ring system expediently has 5-7 ring members, preferably 5 or 6 ring members with one O atom, but additional saturated or unsaturated ring systems, particularly benzene rings, can be used to this ring system. Examples of substances from this class are furan, as well as mono- to
20 tetra-substituted furans, as well as the dihydro and tetrahydro compounds derived from them, for example, tetrahydrofuran. Other cyclic ethers are 1,2- and 1,4-pyrans and their di- and tetrahydro derivatives; finally 1,4-pyrones and their di- and tetrahydro derivatives are also possibilities for the anodic alkoxylation. 1,2-pyrones, which are lactams, can also be alkoxyated. Among the substituents are in particular alkyl groups, which in turn can have a
25 functional groups like hydroxyl, acetoxy, alkoxy carbonyl, amidocarbonyl, carboxyalkyl, nitrile, and amino. Expediently, such a functional group is bonded to the heterocyclic ring via a methylene or ethylene bridge. Other substituents are alkoxy, halogen, carboxyl, acyl and the aldehyde group. If nonaromatic cyclic ethers are alkoxyated, they must have at least one abstractable H atom on a C atom adjacent to the ether oxygen.

30 [0027] When furan or a substituted furan is used the corresponding 2,5-dihydro-2,5-dialkoxyfurans are formed in a generally high material yield and very high

current yield by the anodic alkoxylation in accordance with the invention. Starting from the hydrogenated furans or other cyclic ethers like pyrans, pyrones, dioxane and morpholine the corresponding mono- and/or dialkoxy derivatives are formed where the alkoxy groups are at the carbon(s) adjacent to the ether oxygen.

5 **[0028]** According to another embodiment of the method in accordance with the invention linear and cyclic N-substituted amides can be alkoxyated. The amide nitrogen atom has 1 or 2 alkyl substituents that can also form a saturated or unsaturated, optionally heteroaromatic ring with the N atom. Here at least one C atom bonded to the nitrogen has at least one abstractable hydrogen atom, or the nitrogen atom is a ring member of a
10 heteroaromatic ring.

[0029] Examples of such amides are lactams with 5-7 ring members, where the amide nitrogen can additionally be alkylated.

[0030] The lactams are, for example, N-alkylpyrrolidones, where the heterocyclic ring can additionally contain one or more substituents. The alkyl group bonded to the
15 nitrogen is, especially preferably, methyl. Other examples are N-alkylvalerolactam and N-alkylcaprolactam.

[0031] Another class of substances that consists of N-acylated saturated and unsaturated N-heterocycles, which have at least one abstractable hydrogen atom bonded to the carbon atoms adjacent to the nitrogen or are heteroaromatic. Examples of this class are:
20 N-acylated pyrroles, pyrrolines, and pyrrolodines that are optionally substituted one or more times. The acyl group is, for example, formyl, acetyl, propionyl, benzoyl. The substituents that are bonded to one or more carbon atoms of the N-heterocyclic ring are those substituents that were listed previously in connection with the cyclic ethers. The substituents are especially preferably an alkyl group with 1-4 C atoms, especially methyl or ethyl,
25 hydroxymethyl, acetoxymethyl, and carboxymethyl.

[0032] Finally, open-chain N-alkyl- or N,N-dialkyl fatty acid amides, especially amides of fatty acids with 1 to 6 carbon atoms, can be alkoxyated. Also usable are substrates that have two N-alkylamide structural elements in the molecule.

[0033] According to another embodiment, ketones with a methyl group or methylene
30 group bonded to the carbonyl carbon atom are alkoxyated, especially methoxylated or

ethoxylated. Examples are aliphatic ketones with 3-12 carbon atoms, aromatic-aliphatic ketones like acetophenone and methyl benzyl ketone. Usually, the resulting alkoxyketones are converted directly to the corresponding ketal.

5 [0034] According to another embodiment, alkylated aromatic and heteroaromatic compounds are alkoxyated, where the carbon atom of an alkyl group bonded to an aromatic or heteroaromatic compound must have at least one abstractable hydrogen atom. The substrates can additionally have substituents other than alkyl. Expediently, the aromatic or heteroaromatic compound contains one or more alkyl groups from among methyl, ethyl, and n-propyl. The corresponding alkoxyalkylaromatic or alkoxyalkyl-heteroaromatic compounds
10 result from the alkoxylation in accordance with the invention.

[0035] Compared to the closest prior art, the current yield could be increased considerably through the use of the membrane electrode assembly in accordance with the invention. It turned out that a membrane coated on both sides with carbon black in the described way provided the best results. Under the selected test conditions, there was only a
15 slight increase of the operating voltage. In addition, it was not necessary to add water or cosolvents in order to reduce the voltage to a practical level.

Example 1

[0036] The reactor used in the following example had a structure similar to a fuel cell. A membrane electrode assembly with an electrode surface of 50 cm² per electrode was used.
20 The MEA consisted of a cation exchanger membrane, specifically Nafion® 117, and carbon black particles imbedded in Nafion® on both sides. Carbon black particles that were doped with platinum or with platinum-ruthenium particles were used in other experiments. The MEA was prepared in the manner described above. The membrane was put into contact with graphite paper as current collector on both sides. The electrolyte was circulated in the
25 described batch process successively, i.e., first pumped into the anode space and from there directly into the cathode space and then back to the anode space, until the desired conversion was achieved.

[0037] 17.25 g furan in 70.7 g methanol was galvanostatically electrolyzed at an electrolyte temperature of 10°C and a current density of 50 mA/cm² to a charged conversion
30 of 60% of the theoretically necessary charge amount. At this point the furan was nearly

completely reacted, or evaporated through the open system for purposes of H₂ separation. The composition of the product mixture was determined by calibrated GC and calibrated HPLC. The following table shows the results.

Compound	Efficiency (%)
2,5-dihydro-2,5-dimethoxyfuran	84
1,1,4,4-tetramethoxy-cis-2-butene	12
1,1,4,4-tetramethoxy-trans-2-butene	2
4,4-dimethoxy-crotonic acid methyl ester	1-2
1,1,4,4-tetramethoxybutane	about 1
	about 99